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Potentiometric sensors for the selective determination of sulbutiamine

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Abstract

Five novel polyvinyl chloride (PVC) matrix membrane sensors for the selective determination of sulbutiamine (SBA) cation are described. These sensors are based on molybdate, tetraphenylborate, reineckate, phosphotun gestate and phosphomolybdate, as possible ion-pairing agents. These sensors display rapid near-Nernstian stable response over a relatively wide concentration range 1×10^{-2}–1×10^{-6} M of sulbutiamine, with calibration slopes 28–32.6 mV decade^{-1} over a reasonable pH range 2–6. The proposed sensors proved to have a good selectivity for SBA over some inorganic and organic cations. The five potentiometric sensors were applied successfully in the determination of SBA in a pharmaceutical preparation (arcalion-200) using both direct potentiometry and potentiometric titration. Direct potentiometric determination of microgram quantities of SBA gave average recoveries of 99.4 and 99.3 with mean standard deviation of 0.7 and 0.3 for pure SBA and arcalion-200 formulation respectively. Potentiometric titration of milligram quantities of SBA gave average recoveries of 99.3 and 98.7% with mean standard deviation of 0.7 and 1.2 for pure SBA and arcalion-200 formulation, respectively. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

Sulbutiamine (*N,N'*-[dithiobis [2-(2 hydroxyethyl)1-methyl vinylene]]bis[*N*-[4-amino-2-methyl-5pyridinyl)methyl]formamide] *O,O*-diisobutyrate) is a vitamin, used for the treatment of asthenia in all its forms. It is a thiamine derivative obtained from free thiamine by three structural modifications [1,2]. A polarographic determination of thiamine disulphide in combination with other vitamins has been described [3,4]. A pre-column reduction of disulphides to thiamine with cystine followed by chromatographic analysis of thiamine residues has been reported [5–7]. A colourimetric method for the determination of thiamine disulphides involving derivatization with 2,6-dichloro-*p*-benzoquinone-4-chlorimine has also been published [8]. The disadvantages of these techniques were the poor sensitivity obtained or the non-specificity of the analysis. An HPLC method for a sensitive determination of sulbutiamine has been described [9]. On the other hand, measurements based on

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potentiometric sensors have been thoroughly investigated and proved to offer the advantages of simplicity, accuracy and convenience. Moreover the successful applications of such sensors in pharmaceutical analysis is well documented [10]. However, a literature search showed that no potentiometric sensors for SBA have been published to date. Therefore, the aim of the present work was to develop polymeric ion selective sensors for SBA determination in pharmaceutical formulations.

2. Experimental

2.1. Instrumentation

Perkin–Elmer (Norwalk, CT, USA) 1430 ratio recording IR spectrophotometer using the KBr technique is used for structure elucidation of the ion–pair complexes. The potentiometric measurements were made at $25 \pm 1°C$, using an Orion Model A 720 digital pH–mV meter and Orion Ross combination pH electrode (Model 81-02) for all pH measurements. Sulbutiamine PVC matrix membrane sensors in conjunction with double junction Ag/AgCl reference electrode (Orion Model 90-02) containing KNO_3 (10% W/V) in the outer compartment were used for all potentiometric measurements as the sensor system. Solid state Ag/Ag_2S membrane electrode (Orion Model 94-16) in conjunction with a double junction Ag/AgCl reference electrode were used for the potentiometric standardization of sodium tetraphenylborate (NaTPB) solutions versus standard 1×10^{-2} M $AgNO_3$ solution.

2.2. Reagents and materials

Sulbutiamine and thiamine hydrochloride were obtained from Technologie serier (Orleáns, France). NaTPB, ammonium reineckate, ammonium heptamolybdate, phosphomolybdic and phosphotungestic acids, were purchased from Sigma (St. Louis, MO). Polyvinyl chloride (PVC), tetrahydrofuran (THF), and dioctylphthalate (DOP) were obtained from (BDH) Pool, Dorset, UK). Arcalion-200, the drug formulation of sul-

butiamine was purchased from local drug stores. All other chemicals were of analytical reagent grade. Doubly distilled water (DDW) was used throughout the experiments. A stock solution of sulbutiamine 1×10^{-2} M was prepared by dissolving 0.702 g SBA in a minimum amount of 1×10^{-1} M HCl and completing the resulting clear solution (pH $\approx$ 3) to 100 ml with (DDW). Dilute SBA solutions $(1 \times 10^{-3}–1 \times 10^{-6}$ M) were freshly prepared by accurate dilution with DDW and kept in brown stoppered bottles. These solutions were used for the calibration of SBA sensors based on molybdate, tetraphenylborate, and phosphotungestate. Sensors based on reineckate and phosphomolybdate were calibrated in background of 10^{-1} M KCl and potassium hydrogenphthalate (pH 4.0; 0.05 M), respectively. A standard solution of NaTPB was prepared by dissolving 1.71 g in a minimum volume of (DDW). The solution was then filtered, transferred to a 500-ml volumetric flask and diluted to the mark. The solution was standardized potentiometrically versus standardized 1×10^{-2} M silver nitrate solution using Ag/Ag_2S solid-state membrane electrode system for endpoint detection. Arcalion-200 solution was prepared by pulverizing ten tablets to fine powder, and an accurate weight equivalent to 0.1 tablet was transferred into 25 ml beaker containing 20 ml of (DDW), and the pH of solution was adjusted to pH $\approx$ 3 with 10^{-1} M HCl. The solution was transferred to 25-ml volumetric flask, completed, to the mark by (DDW), shaken well and stored in a brown stoppered bottle.

2.3. Membrane and sensor preparation

Sulbutiamine ion–pair complexes were prepared by mixing aliquots, 40 ml of 1×10^{-2} M of the reagents used with 10-ml aliquots of 1×10^{-2} M SBA solution. Each solution mixture was stirred for 10 min, the resulting precipitates were filtered off by suction, washed with DDW, dried at ambient temperature for 24 h. Elemental analysis data of the ground precipitates, SBA–molybdate (I), SBA–TPB(II), SBA–reineckate (III), SBA–phosphotungestate (IV) and SBA–phosphomolybdate (V) agreed with SBA–reagent ion–

pair composition as shown in Table 1. The I.R. spectra of the dried ion-pairs show that the high frequency bands exhibited by sulbutiamine base for the N–H stretching vibrations at ≈ 3400 and 3500 cm^{-1} are markedly broaden and lie between 2500–3141 cm^{-1}, which reveals the formation of the amine salt. Master PVC membranes of approximately 0.1 mm thick were prepared and fitted to the sensor's body as previously described [11,12]. The internal reference solution was prepared by mixing equal volumes of 1×10^{-2} M

3. Results and discussion

3.1. Characterization and evaluation of the SBA sensors

SBA–reagent ion–pair precipitates were prepared, characterized and examined as novel electroactive materials in PVC matrix as membranes responsive to SBA cation. The performance characteristics Table 2 of the sensors proposed were evaluated, according to IUPAC recommendations [13] using the following electrochemical cell.

Ag / AgC1	1×10^{-2} M NaCl	PVC	SBA		10% KCl	
	1×10^{-2} M SBA	Membrane	Test solution			Ag/AgCl
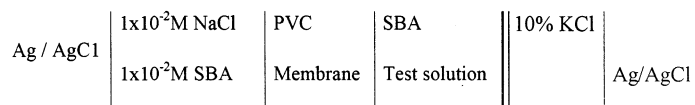
SBA and NaCl solutions. These sensors were conditioned by soaking in (DDW) for 3 h before use and stored in (DDW) when not in use.

2.4. Calibration

The proposed sensors were calibrated individually by measuring the e.m.f. values after stabilization to ± 0.2 mV in a series of SBA solutions covering the concentration range 10^{-6}–10^{-2} M SBA. The e.m.f. values were plotted on a semilogarithmic paper as a function of SBA concentration. These calibration graphs were used for subsequent determination of unknown SBA concentrations.

The proposed sensors exhibit rapid linear and stable potentiometric response in the concentration range 1×10^{-2}–1×10^{-4} M using sensor III and V and extends down to 1×10^{-6} M for sensor IV. The reproducibility and stability of these sensors were evaluated by constructing replicate calibration graphs ($n = 10$) over a period of 2 weeks. The potential displayed by the proposed sensors for consecutive measurements in the previously mentioned concentration range of SBA solutions in the same day do not vary by more than ± 0.2 mV ($n = 5$). Changes in the calibration slopes do not exceed ± 0.3 mV decade^{-1} of SBA concentration. The dynamic response time of these sensors was tested by measuring the time

Table 1
Elemental analysis data of sulbutiamine ion–pair complexes[a]

Ion pair complex	C (%)		H (%)		N (%)	
	Calculated	Found	Calculated	Found	Calculated	Found
SBA [(NH$_4$)$_5$ Mo$_7$O$_{24}$]$_2$	12.81	12.99	2.90	2.90	8.40	8.19
SBA [Cr (SCN)$_4$(NH$_3$)$_2$]$_2$	35.79	36.0	4.47	4.24	20.87	20.71
SBA [B(C$_6$H$_5$)$_4$]$_2$	71.52	72.11	6.56	6.47	8.35	8.60
SBA [H$_2$PO$_4$.12 WO$_3$]$_2$	5.90	6.35	0.80	0.93	1.7	1.95
SBA [H$_2$PO$_4$.12 MoO$_3$]$_2$	8.80	9.43	1.19	1.29	2.57	2.78

[a] SBA represents C$_{32}$H$_{48}$N$_8$O$_6$S$_2$.

Table 2
Response characteristics of sulbutiamine PVC membrane sensors at $25 \pm 2°C^a$

Parameter	Value				
	Sensor I	Sensor II	Sensor III	Sensor IV	Sensor V
Slope, (mV decade^{-1}) $\pm$ SD	27.95 ± 0.5	31.3 ± 0.2	29.1 ± 0.5	30.6 ± 0.3	32.6 ± 0.2
Usable range, (M)	$10^{-5}-10^{-2}$	$10^{-5}-10^{-2}$	$10^{-4}-10^{-2}$	$10^{-6}-10^{-2}$	$10^{-4}-10^{-2}$
Correlation coefficient, (r)	0.998	0.999	0.997	0.997	0.995
Intercept, (mV) $\pm$ SD	224.9 ± 0.9	249 ± 0.6	244.8 ± 0.6	208.4 ± 0.5	215.9 ± 0.3
Lower limit of the linear range, (M) $\pm$ SD	1 ± 0.01 $\times 10^{-5}$	1 ± 0.012 $\times 101^{-5}$	1 ± 0.016 $\times 10^{-4}$	1 ± 0.011 $\times 10^{-6}$	1 ± 0.02 $\times 10^{-4}$
Lower limit of detection, (M)	2.5×10^{-6}	4.1×10^{-6}	2.9×10^{-5}	3.0×10^{-7}	2.1×10^{-5}
Working pH range	2–5.8	2–5.45	2–5.8	2–6	2–4.8
Response time for 1×10^{-3} M, (s)	17	16	15	15	20
Life time, (days)	20	25	25	20	20

^{a} Average of ten measurements per 2 weeks.

required to reach a steady potential within ± 0.2 mV. Successive immersion of the sensors in different SBA solutions having a ten-fold difference in concentration is fairly short. They reach 95% of their final steady potentials after 15–20 s for SBA $\geq 10^{-3}$ M and 20–30 s for SBA $< 10^{-3}$ M. The lower limit of detection is obtained as previously described [14].

The effect of pH of SBA test solutions (10^{-3} and 10^{-4} M) on the potential reading of the proposed sensors was examined over a pH range 2–8. The e.m.f.–pH plots revealed that potential readings are insensitive to pH changes over the range between 2 and 5 observed for sensor I and V. This range is extended up to pH 6 for the other sensors. This is probably due to the formation of deprotonated species in the test solution. Fig. 1 represents this effect on the response of sensor III.

The performance of these sensors in the presence of some inorganic and organic cations were measured using the separate solutions method
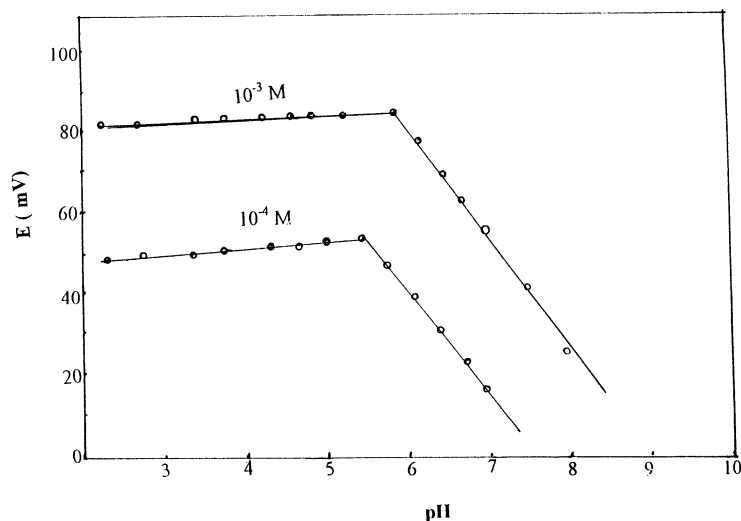

Fig. 1. Effect of pH on the response of sensor (III) in 10^{-3} and 10^{-4} M of SBA solution at 25°C.

Table 3
Potentiometric selectivity coefficient of sulbutiamine PVC membrane sensors

Interferent, C	$K_{SBA2+, C}^{Pot}$				
	Sensor I	Sensor II	Sensor III	Sensor IV	Sensor V
Thiamine HCI	7.5×10^{-4}	6.3×10^{-3}	1.4×10^{-2}	8.2×10^{-3}	1.9×10^{-2}
Thiourea	7.8×10^{-6}	6.4×10^{-7}	1.8×10^{-5}	7.4×10^{-5}	5.9×10^{-3}
L-Cystine	1.9×10^{-2}	2.1×10^{-3}	3.5×10^{-2}	1.6×10^{-2}	8.6×10^{-2}
Glutamic acid	3.3×10^{-4}	1.8×10^{-3}	2.7×10^{-3}	3.6×10^{-3}	6.9×10^{-2}
2-Amino benzoic acid	1.6×10^{-4}	1.1×10^{-4}	8.9×10^{-4}	1.8×10^{-3}	9.5×10^{-2}
Succinimide	1.9×10^{-4}	1.1×10^{-5}	2.3×10^{-4}	1.7×10^{-2}	7.4×10^{-2}
Glucose	6.9×10^{-5}	3.6×10^{-4}	1.8×10^{-3}	3.5×10^{-3}	8.9×10^{-2}
Ag^+	5.8×10^{-4}	3.1×10^{-5}	6×10^{-3}	1.6×10^{-4}	2.7×10^{-2}
K^+	7.1×10^{-3}	2.3×10^{-4}	5.2×10^{-3}	1.2×10^{-3}	2.1×10^{-2}
Ba^{2+}	7.5×10^{-4}	1.2×10^{-3}	8.9×10^{-2}	5.2×10^{-3}	9.4×10^{-2}

[15–17]. The obtained values for the selectivity coefficient $K_{SBA2+, C}^{Pot}$ are listed in Table 3. These data show that the interfering effect of a smaller related moiety of SBA, i.e. thiamine showed not to have a serious interfering effect. Calibration graphs of sensor IV were constructed at different test solution temperature 10–65°C using a thermostated cell. Fig. 2, shows that within the investigated temperature range, the sensor responds practically to SBA concentration with a nearly constant usable concentration range of about

1.0×10^{-6}–1.0×10^{-2} M. The observed deviation from the theoretical Nernstian value is nearly constant and the sensor show high degree of reproducibility. For the determination of the thermal coefficient of the sensor ($dE°/dt$), the standard cell potential ($E°$) was determined from the calibration graphs constructed at 10–65°C-test solution temperature as the intercepts of the calibration graphs at 1 M SBA concentration. Straight-line plot is obtained according to the following equation [18].
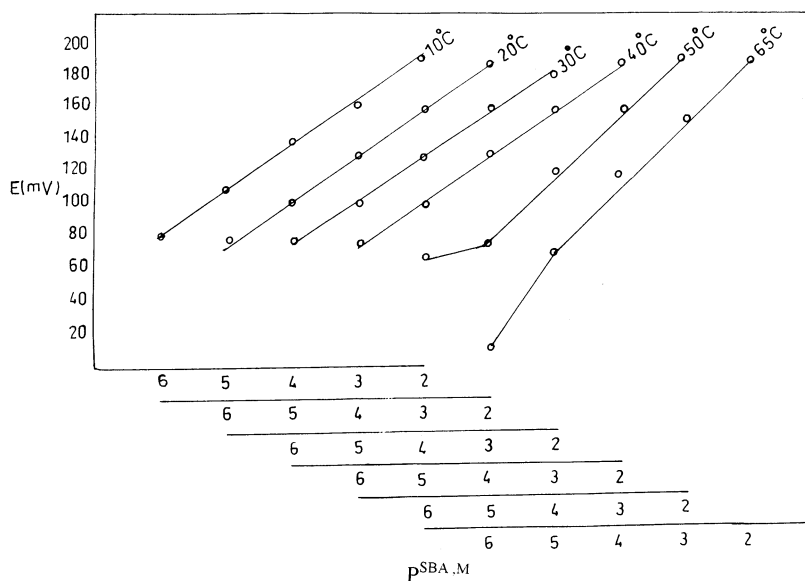

Fig. 2. Calibration graphs of sensor (IV) at test solution temperatures 10–65°C.

Table 4
Direct potentiometric, spiking and potentiometric titration of SBA and arcalion using SBA–PVC membrane sensors

Sensor	Recovery %, $\pm$ SD[a]					
	Direct Potentiometry		Spiking		Potentiometric titration	
I	98.9 ± 0.3	101.1 ± 0.01	99.1 ± 0.11	99.7 ± 0.8	99.3 ± 1.2	98.2 ± 1.5
II	99.3 ± 0.06	97.9 ± 1.0	99.9 ± 0.2	98.3 ± 1.1	100.0 ± 0.66	99.1 ± 1.4
III	98.6 ± 0.7	98.8 ± 0.5	99.3 ± 0.6	99.0 ± 0.4	98.6 ± 0.57	98.0 ± 1.13
IV	100.1 ± 0.09	99.4 ± 0.1	100.0 ± 0.2	100.2 ± 0.05	99.5 ± 0.18	99.8 ± 0.94
V	99.9 ± 0.2	98.6 ± 0.41	100.01 ± 0.5	99.3 ± 0.09	99.0 ± 0.96	98.4 ± 0.89

[a] Average of three measurements.

$$E_0 = E_{25} + (dE^{o}/dt)\ (t - 25)$$

The slope of the straight line obtained represents the thermal coefficient of the sensor, amounting to 0.31 mV°C^{-1} revealing a fairly good thermal stability of the sensor within the investigated temperature range.

3.2. Analytical application

The reliability of the proposed sensors for SBA determination in pharmaceutical products was assessed using the available SBA formulation (arcalion-200). Aqueous solutions of pure SBA and arcalion-200 containing 7.0 µg ml^{-1}–7.0 mg ml^{-1} were prepared and analyzed by direct potentiometry using each of the five SBA membrane sensors. The displayed potentials were compared with the corresponding calibration graphs constructed at the same day to assess the accuracy and reproducibility. The obtained results, Table 4 gave average recoveries of 99.4 and 99.3% with mean standard deviations of 0.7 and 0.3% for pure SBA and arcalion-200 solutions, respectively. The above test solutions were also determined by the standard addition method, spiking technique [19,20]. The results obtained gave average recoveries of 99.5 and 99.1% with mean standard deviations of 0.9 and 0.5% for pure SBA and arcalion solutions, respectively Table 4. Potentiometric titrations of 10 ml aliquots of 1×10^{-3} M SBA solutions containing 7.029 mg were examined, using each of the proposed SBA sensors for end point detection and NaTPB, ammoniummolybdate, ammoniumreinecate, phosphotungestic acid and phosphomolybdic acid as titrants. Typical potentiometric titration curves using the proposed sensor systems with standard 1×10^{-2} M NaTPB as titrant were plotted. Inflection breaks of 100–120 mV at points corresponding to stoichiometry of 1 SBA:2 TPB were obtained. Fig. 3 represents the titration curves obtained using sensor I, curve (a) represents the potential versus volume, where (b) represents $\Delta E/\Delta V$ versus V. Three replicates of measurements Table 4, for the five sensors were performed, the average recoveries were 99.3 and 98.7% with standard deviations of 0.7 and 1.2% for pure SBA and arcalion-200 solutions, respectively.
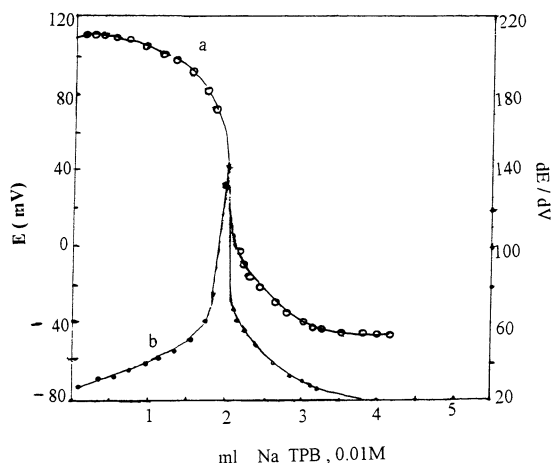

Fig. 3. Typical potentiometric titration curve for 1 ml of 1×10^{-2} M SBA with standard 1×10^{-2} M NaTPB using sensor (I). (a) Potential versus volume. E/V. (b) $\Delta E/\Delta V$ versus V.

4. Conclusion

Despite the accuracy of the previously reported methods for sulbutiamine determination, the proposed potentiometric sensors, provide a simple low-cost method, which offers a direct selective determination of SBA in pure solutions and in its pharmaceutical formulation without prior separation or derivatization steps with high accuracy, precision and sensitivity.

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